Ovarian cancers commonly exhibit upregulation of the PI3K/mTOR signaling. Using a genetically engineered ovarian cancer mouse model (Pten deletion;KrasG12D), Kinross and colleagues show that PF-04691502, a PI3K and mTOR inhibitor in clinical development, potently inhibits PI3K/mTOR signaling, FDG-PET activity, and inhibits tumor growth in vivo. However, PF-04691502 exhibited only short-term benefit as a single agent. Long-term therapeutic benefit could be achieved through combined therapy of PF-04691502 with MEK inhibitor PD-0325901, which, via coordinated activation of apoptosis, led to tumor regression. This study identifies combination PF-04691502 and PD-0325901 therapy as a promising new approach for the treatment of ovarian cancers.

Triple-negative breast cancers have the worst prognosis of any subset of breast cancer, at least in part because of a lack of viable therapeutic targets. Epidermal growth factor receptor (EGFR) is overexpressed in approximately 50% of triple-negative breast cancers, but attempts at targeting this receptor in clinical trials have, to date, produced disappointing results. Liu and colleagues show that mTOR inhibition in combination with EGFR inhibition leads to synergistic effects in triple-negative breast cancers in vitro and suppressed tumor growth in vivo. They are currently evaluating the combination of the EGFR inhibitor, lapatinib, and the mTOR inhibitor, everolimus, in patients with metastatic triple-negative breast cancer.

Misexpression of microRNAs (miRNA) is widespread in human cancers, with aberrations including overexpression of oncogenic miRs and downregulation of tumor suppressor miRs (TSG-miR). Pramanik and colleagues developed a method of restituting expression of downregulated TSG-miRs in vivo using a lipid-based nanoparticle for systemic delivery of miRNA expression vectors (nanovector). Selecting two candidate TSG-miRs (miR-34a and the miR-143/145 cluster), the authors show the usefulness of the nanovector platform—one with potential broad applicability in systemic miRNA delivery to cancer cells—in both subcutaneous and orthotopic xenograft models of pancreatic cancer.
Highlights of This Issue

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